ISRCTN96273644 https://doi.org/10.1186/ISRCTN96273644

A study to see how effective the drug Axitinib is at preventing cancer cells from growing and to see if this means that patients with kidney cancer require less extensive surgery

Submission date
13/02/2017

Recruitment status
No longer recruiting

Registration date
01/03/2017

Overall study status
Completed

Last Edited
10/10/2022

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-axitinib-for-kidney-cancer-naxiva

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2017-000619-17

IRAS number

ClinicalTrials.gov number
NCT03494816

Secondary identifying numbers
NAXIVA 2.0 (06/06/2018)

Study information

Scientific Title
Phase II neoadjuvant study of Axitinib for reducing extent of venous tumour thrombus in clear cell renal cell cancer with venous invasion

Acronym
NAXIVA

Study objectives
A reduction in the extent of the venous tumour thrombus, as assessed by the Mayo classification, will potentially result in less extensive and less morbid surgical approach with immediate patient benefits of reduced operative mortality/morbidity, potential shorter hospital stay and shorter recuperation period to return to full activities of daily living.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England – Cambridgeshire and Hertfordshire Ethics Committee, 02/08/2017

Study design
Single-arm single-agent open label phase II feasibility study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Clear cell renal cell cancer with venous thrombus invasion

Interventions
All participants will receive an 8 week course of Axitinib. Patients will be followed up every 2 weeks from day 1, week 1 of receiving Inlyta. All patients will start at 5mg BID with possible escalation to 7mg BID and the max 10mg BID. Only if no adverse events related to study drug above CTCAE grade 2 for a consecutive 2-week period the patient may have their dose increased by one dose level to a maximum of 10 mg BID. Patients will be given a 2 week supply at each follow up visit of Inlyta (oral tablet) to be taken twice daily as per instructed.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Axitinib

Primary outcome measure
Thrombus invasion will be measured using MRI scanning according to the Mayo classification at baseline and pre-surgery (week 9).

Secondary outcome measures
Current secondary outcome measures as of 23/04/2018:
1. Percentage change in surgical approach (to a less invasive surgical approach) as assessed by review of MRI scans by surgeons at baseline and week 9 (i.e after axitinib therapy has been completed)
2. Percentage change in height of the cancer invasion into the large blood vessels draining the kidney (venous tumour thrombus). This will be evaluated by comparing baseline and week 9 scans. Local radiologists will conduct the evaluation and a central radiology review will be conducted.

3. Objective tumour response rate measured by MRI/CT scans at baseline and week 9.
4. Complications of surgery (i.e. blood loss and need for a blood transfusion) assessed according to the Clavien-Dindo classification of surgical complications at baseline and week 9

Previous secondary outcome measures
1. Percentage change in surgical approach is assessed by review of MRI scans by surgeons at baseline and 9 weeks
2. Percentage change in height of the venous tumour thrombus will be evaluated by comparing baseline and week 9 scans. Local Radiologists will conduct the evaluation and a central radiology review will be conducted.
3. The response rate (RECIST) will be measured by MRI/CT at baseline and week 9
4. Change in Inferior vena cava- tumour thrombus volume will be assessed by radiologists comparing CT/MRI scans taken at baseline and week 9
5. Morbidity will be measured using MRI/CT scanning according to the Clavien-Dindo classification at baseline and week 9

Overall study start date
01/03/2017

Completion date
10/06/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/02/2019:
1. Aged 18 years and over
2. Biopsy-proven clear cell RCC
3. Immediate resection of the primary tumour considered technically possible
4. The patient must be suitable for and willing to undergo nephrectomy surgery
5. The clinical (radiologically determined) stage of the tumour must be into the main renal vein (cT3a, but seen in the main branch of the renal vein leading to but not beyond the vein ostium with the inferior vena cava (IVC)), or the IVC itself either below of above the diaphragm (cT3b or cT3c respectively)
6. Nodal status may be clinically node negative (cN0) on CT, indeterminate (cNx) or clinically node positive on CT (cN1)
7. Non-metastatic (M0) and metastatic (M1) clear cell renal cell patients
8. The patient must have an ECOG performance status of either 0 or 1
9. Urine must contain less than 2 g protein. If urine contains ≥2 g then a 24-h urine collection or urinary protein creatinine ratio (PCR) should be performed and the patient may enter NAXIVA only if urinary protein is <2g per 24 hours or PCR <200mg/mmol.
10. Serum Creatinine ≤1.5xULN or estimated Creatinine clearance ≥30mL/min as calculated using the Cockcroft- Gault (CG) equation.
11. All female patients with reproductive potential must have a negative serum or urine pregnancy test within a maximum of 14 days prior to starting trial treatment.

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1. Aged 18 years and over
2. Biopsy-proven clear cell RCC
3. Immediate resection of the primary tumour considered technically possible
4. The patient must be suitable for and willing to undergo nephrectomy surgery

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6. Nodal status may be clinically node negative (cN0) on CT, indeterminate (cNx) or clinically node positive on CT (cN1)
7. Non-metastatic (M0) and metastatic (M1) clear cell renal cell patients
8. The patient must have an ECOG performance status of either 0 or 1
9. Urine must contain less than 2 g protein. If urine contains ≥2 g then a 24-h urine collection should be performed and the patient may enter if urinary protein is <2 g per 24 hours.
10. All female patients with reproductive potential must have a negative serum or urine pregnancy test within a maximum of 14 days prior to starting trial treatment.

Previous inclusion criteria:
1. Aged 18 years and over
2. Biopsy proven clear cell RCC
3. Resectable Tumour
4. The clinical (radiologically determined) stage of the tumour must be into the main renal vein (cT3a, but seen in the main branch of the renal vein leading to but not beyond the vein ostium with the inferior vena cava (IVC)), or the IVC itself either below of above the diaphragm (cT3b or cT3c respectively)
5. Nodal status may be clinically node negative (cN0) on CT, indeterminate (cNx) or clinically node positive on CT (cN1)
6. Non-metastatic (M0) and Metastatic (M1) clear cell renal cell patients
7. Stratification by the Mayo classification

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
20 patients will be recruited over a 24 month period in 6-8 sites across the UK.

Total final enrolment
21

Key exclusion criteria
Current exclusion criteria as of 11/02/2019:
1. Metastatic patients with poor risk on the Memorial Sloan Kettering Cancer Centre (MSKCC) score and deemed suitable for cytoreductive nephrectomy at time of enrolment
2. Other invasive malignancy within the last 2 years. Patients with previous history of malignancies with a negligible risk of metastasis or death and treated with expected curative intent are eligible, for example but not exclusively:

2.1. Carcinoma in situ of the cervix.
2.2 Basal or squamous cell skin cancer.
2.3 Localized low to intermediate risk prostate cancer treated with curative intent and absence of prostate specific antigen (PSA) relapse; or prostate cancer (Stage T1/T2a, Gleason ≤6 and PSA
3. Women who are pregnant or are breastfeeding. Female patients must be surgically sterile, be postmenopausal, or must agree to use effective contraception during the period of therapy. All female patients with reproductive potential must have a negative pregnancy test (serum or urine) prior to enrolment. Male patients must be surgically sterile or must agree to use effective contraception during the period of therapy.
4. Current signs or symptoms of severe progressive or uncontrolled hepatic, endocrine, pulmonary disease other than directly related to RCC
5. Gastrointestinal abnormalities including:
5.1. Inability to take oral medication
5.2. Requirement for intravenous alimentation
5.3. Prior surgical procedures affecting absorption including total gastric resection
5.4. Treatment for active peptic ulcer disease in the past 6 months
5.5. Active gastrointestinal bleeding, unrelated to cancer, as evidenced by hematemesis, hematochezia or melena in the past 3 months without evidence of resolution documented by endoscopy or colonoscopy
5.6. Malabsorption syndromes
6. Current use or anticipated need for treatment with drugs that are known potent CYP3A4 inhibitors (see section 8.12, concomitant therapy)
7. Current use or anticipated need for treatment with drugs that are known CYP3A4 or CYP1A2 inducers (see section 8.12, concomitant therapy)
8. Requirement of anticoagulant therapy with oral vitamin K antagonists. Low-dose anticoagulants for maintenance of patency of central venous access device or prevention of deep venous thrombosis is allowed. Therapeutic use of low molecular weight heparin is allowed.
9. Active seizure disorder, spinal cord compression, or carcinomatous meningitis
10. Any of the following within 12 months prior to study entry:
10.1 myocardial infarction
10.2 uncontrolled angina
10.3 coronary/peripheral artery bypass graft
10.4 symptomatic congestive heart failure
10.5 cerebrovascular accident or transient ischemic attack
11. Uncontrolled hypertension (>160/100 mmHg despite optimised antihypertensive treatment)
12. Known human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS)-related illness
13. ALT or AST ≥1.5 x upper limit of normal; Bilirubin ≥1.5 x upper limit of normal
14. Serum creatinine ≥1.5 x upper limit of normal
15. Neutrophil count <1.0 x 10(9)/l; platelet count <100 x 10(9)/l; Hb ≤90 g/l
16. Known severe hepatic impairment (Child-Pugh class C)
17. Known hypersensitivity to axitinib or any of its excipients. Specifically patients with hereditary galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not enter the study.

Previous exclusion criteria as of 23/04/2018:
1. Metastatic patients with poor risk on the Memorial Sloan Kettering Cancer Centre (MSKCC) score and deemed suitable for cytoreductive nephrectomy at time of enrolment
2. Presence of active second malignancy. Patients will be eligible if they have adequately treated basal cell carcinoma, squamous cell skin cancer, in situ cervical cancer, stable prostate cancer or if treated with curative intent for any other cancer with no evidence of disease for 2 years.
3. Women who are pregnant or are breastfeeding. Female patients must be surgically sterile, be

postmenopausal, or must agree to use effective contraception during the period of therapy. All female patients with reproductive potential must have a negative pregnancy test (serum or urine) prior to enrolment. Male patients must be surgically sterile or must agree to use effective contraception during the period of therapy.
4. Current signs or symptoms of severe progressive or uncontrolled hepatic, endocrine, pulmonary disease other than directly related to RCC
5. Gastrointestinal abnormalities including:
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15. Neutrophil count <1.0 x 10(9)/l; platelet count <100 x 10(9)/l; Hb ≤90 g/l
16. Known severe hepatic impairment (Child-Pugh class C)
17. Known hypersensitivity to axitinib or any of its excipients. Specifically patients with hereditary galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not enter the study.

Previous exclusion criteria
1. The presence of active second malignancy. Patients will be eligible if they have adequately treated basal cell carcinoma, squamous cell skin cancer, in situ cervical cancer, stable prostate cancer or if treated with curative intent for any other cancer with no evidence of disease for 2 years.
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pulmonary disease other than directly related to RCC.
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5.2. Requirement for intravenous alimentation
5.3. Prior surgical procedures affecting absorption including total gastric resection
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11. Known human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS)-related illness

Date of first enrolment
01/12/2017

Date of final enrolment
06/01/2020

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Addenbrooke's Hospital
Cambridge Biomedical Campus
Hill's Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
Royal Marsden
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
St George's Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Broomfield Hospital
Court Road
Broomfield
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
The Royal Free Hospital
Pond St.
Hampstead
London

United Kingdom
NW3 2QG

Sponsor information

Organisation
Common Services Agency

Sponsor details
Strategic Business Unit
Public Health and Intelligence (Information Services Division)
Gyle Square
South Gyle Crescent
Edinburgh
United Kingdom
EH12 9EB

Sponsor type
Government

ROR
https://ror.org/04za2st18

Funder(s)

Funder type
Industry

Funder Name
Pfizer UK

Alternative Name(s)
Pfizer Ltd, Pfizer Limited

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-review journal.

Intention to publish date
01/07/2022

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	ClinicalTrials.gov	30/06/2021	23/05/2022	No	No
Basic results	EU-CTR	23/05/2021	16/06/2022	No	No
Results article		23/06/2022	29/07/2022	Yes	No
Protocol file	version 2.0	06/06/2018	10/10/2022	No	No